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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/389,537	09/02/1999	PATRICK V. WARREN	DIVER1240-3	5543

7590

06/04/2002

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 06/04/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/389,537

Applicant(s)

WARREN ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 17-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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### **DETAILED ACTION**

The amendment filed March 22, 2002 (deposited with the United States Postal Service on December 3, 2001) amending the specification to correct clerical errors, amending claims 17-27 and adding claims 28 and 29 has been entered.

The Sequence Listing and the computer readable form thereof filed April 3, 2002 have been entered.

Claims 17-29 are pending.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection has been explained in the Office action mailed July 3, 2001.

In sum, the genus of aminotransferases/transaminases is highly variant. The specification does not disclose the correlation between structure and specific function common to the members of the genus. "Transaminase or aminotransferase" encompass

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diverse enzymes having any substrate and stereo specificity. While the claims impart a structural limitation (70, 80, 90 or 95%), there is no specific functional limitation.

Claims 17-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transaminase or aminotransferase having amino acid sequences as set forth in SEQ ID NOs: 25-32, does not reasonably provide enablement for a transaminase or aminotransferase of unspecified specificity having an amino acid sequence 70, 80, 90 or 95% identical to SEQ ID NOs: 25-32 and a method of use thereof as well as for a transaminase or aminotransferase of a known specificity having an amino acid sequence 70% identical to SEQ ID NOs: 25-32 and a method of use thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

This rejection has been explained in the Office action mailed July 3, 2001.

Claims 28 and 29 are included in the rejection because the following considerations are specifically underscored.

The claims are drawn to enzymes having the 30% of their structure different from the enzymes having the sequences of SEQ ID NOs: 25-32. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the

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desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

The specification does not support the broad scope of the claims because the specification does **not** establish regions of the protein structure which may be modified without effecting a specific aminotransferase activity.

Despite knowledge in the art to produce mutations in proteins and the isolation of DNA molecules, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to and/or delete from the known sequence), changes in amino acid residues will result in a specific transaminase or aminotransferase activity (i.e., specific amino acid donor and acceptor). Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The state of the art does not allow the predictability of the properties based on the structure. The amino acid sequence of a protein determines its structural and functional properties and knowledge of which residues can be altered or removed, so that they retain 70% identity, and result in a specific activity is well outside the realm of routine experimentation.

Furthermore, with regard to claim 29, the specification does not teach how to modify the sequence of the parent enzyme to impart the ability to transfer an amino

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group from an amino acid to  $\alpha$ -keto acid if the parent enzyme does not exhibit said function (for example, SEQ ID NO : 27 and 30-32).

While a method for transferring an amino group from a specific amino acid to an  $\alpha$ -keto acid corresponding to an amino acid to be produced is enabled for some enzymes of SEQ ID NOs: 25-32 according to their specificity, it is not enabled for enzymes of SEQ ID NOs :27 and 30-32, for example.

Therefore, one skilled in the art would require guidance as to how to make a transaminase or aminotransferase of a given specificity with the amino acid sequence that is 70% identical to SEQ ID NOs:25-32 and how to use said enzyme for transferring an amino group from any amino acid to any  $\alpha$ -keto acid in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18, 28 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18, line 4, recites "an enzyme encoded by an amino acid sequence". An enzyme has an amino sequence and is not encoded thereby.

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Claims 28 and 29 recite "enzyme has the same amino group acceptor and amino group donor specificity" without pointing out and distinctly claim the amino group acceptor and donor.

### ***Response to Arguments***

Applicant's arguments filed March 22, 2002 have been fully considered but they are not persuasive.

Applicants argue that "Applicants respectfully submit that the claims, as pending, include both structural and functional requirements for the claimed enzyme. ... The claims are not drawn to any transaminase or aminotransferase, as alleged in Paper No. 12, but to any enzyme that is at least 70% identical to any one of SEQ ID NOS: 25-32 and has transaminase or aminotransferase activity" (page 9). "Any transaminase" in Paper No. 12 refers to a transaminase of any specificity. The genus of transaminases encompasses enzymes with widely different functions and because of that, a functional characteristic such as "transaminase activity" is insufficient.

With regard to the enablement Applicants argue that "Even where there are multiple transaminase or aminotransferase activities, one of skill in the art would have known, at the time of filing of the application, how to determine whether an enzyme with at least 70% homology to any one of SEQ ID NOS: 25-32 has transaminase or aminotransferase activity" (page 10). The examiner agrees that one of skill in the art

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would have known how to determine a specific defined transaminase activity. For example, one of skill in the art would have known how to determine a specific defined transaminase activity of transferring  $\alpha$ -amino group of the 20 L-amino acids to the  $\alpha$ -carbon atom of  $\alpha$ -ketoglutarate (the specification at page 1, last paragraph; page 21, penultimate paragraph, and page 22, penultimate paragraph). However, the examiner disagrees with the notion that one of skill in the art would have known how to determine any possible transaminase or aminotransferase activity.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of



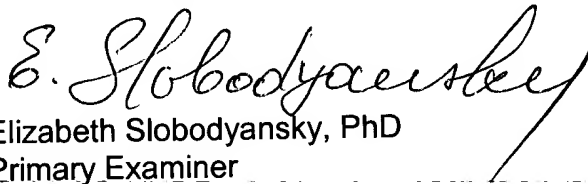
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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.



Elizabeth Slobodyansky, PhD  
Primary Examiner

May 30, 2002